RECEIVED .

TCENLEY 1800!S300 Sheet _ of U.S. Department of Commerce ATTY. DOCKET NO. SERIAL NO. Form 1449 09/597,732 Patent and Trademark Office 2323-151 **APPLICANT** Mark T. KEATING et al. T OF MATERIALS CITED BY APPLICANT (Use several sheets if necessary) FILING DATE GROUP 19 June 2000 1646 U.S. PATENT DOCUMENTS FILING DATE IF **EXAMINER** DOCUMENT DATE NAME CLASS SUBCLASS **APPROPRIATE** INITIAL NUMBER FOREIGN PATENT DOCUMENTS TRANSLATION DOCUMENT COUNTRY SUBCLASS CLASS NUMBER DATE YES NO 9 2 3 5 9 8 07/03/97 wo -C12N XX G01N NON-PATENT DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) Ackerman, M.J. "The Long QT Syndrome: Ion Channel Diseases of the Heart", Mayo Clin. Proc., 1998; Barhanin, J. et al. (1997). GenBank Accession No. AF000571.1 Benhorin, J. et al. "Evidence of Genetic Heterogeneity in the Long QT Syndrome", Science, June 25, 1993; ۍ Bulman "Phenotype variation and newcomers in ion channel disorders", Human Molecular Genetics, 2 1997; 6(10) Review:1679-1685 Chouabe, C. et al. "Properties of KVLQT1 K+ channel mutations in Romano-Ward and Jervell and Lange-Nielsen inherited cardiac arrhythmias", The EMBO Journal, 1997, 16(17):5472-5479 Coonar, et al. "Molecular Genetics of Familial Cardiomyopathies", Advances in Genetics, _ Curran, M. et al. "Locus Heterogeneity of Autosomal Dominant Long QT Syndrome", J. Clin. Invest., August 1993; 92:799-803 de Jager, et al. "Evidence of a long QT founder gene with varying phenotypic expression in South African families", J. Med. Genet., 1996; 33:567-573 1 Donger, C. et al. "KVLQT1 C-Terminal Missense Mutation Causes a Forme Fruste Long-QT Syndrome", Circulation, 1997; 96:2778-2781 Ŷ Hoffman, et al. "Ion Channels - Molecular Divining Rods Hit Their Clinical Mark", New England Journal of Medicine, May 29, 1997; 336(22):1599-1600 2 Itoh, T. et al. "Genomic organization and mutational analysis of KVLQT1, a gene responsible for familial long QT syndrome", Hum. Genet., 1998; 103:290-294 à Keating, et al. "Consistent Linkage of the Long-QT Syndrome to the Harvey Ras-I Locus on Chromosome II", Am. J. Hum. Genet., 1991; 49:1335-1339 7 Keating, M. "Linkage Analysis and Long QT Syndrome Using Genetics to Study Cardiovascular Disease", Circulation, 1992; 85:1973-1986 9 Keating, et al. "Linkage of a Cardiac Arrhythmia, the Long QT Syndrome, and the Harvey ras-1 Gene", Science, May 3, 1991; 252:704-706 DATE CONSIDERED **EXAMINER** DUL 11-20-01

EXAMINER: Initial if reference considered, whether or not citation is in conformation with MPEP 609; Draw line through citation

if not in conformance and not considered. Include copy of this form with next communication to applicant.

17/m Ga

RECEIVED

SEP 0 8 20003

Sheet 2 of 3

		- TECHO	WER ISOMONIO		
Form 1449	U.S. Department of C Patent and Tradem	ommerce	ATTY, DOCKET NO. 2323-151	SERIAL NO. 09/597,732	
PE VOUST	T OF MATERIALS CITED BY APPLICANT		APPLICANT Mark T. KEATING et al.		
0 0 000	(Use several sheets if necessary)		FILING DATE 19 June 2000	GROUP 1646	
A Juge	NON-PATENT DOCUMENTS (Including AL	Author, Title, Date, Pertinent Pages, Etc.)			
7	Komsuoglu, et al. "The Jervell and Lange-Nie 47:189-192	elsen syndr	ome", International Journal o	f Cardiology, 1994;	
	Larsen, L.A., et al. "High-Throughput Single-Strand Conformation Polymorphism Analysis by Automated Capillary Electrophoresis: Robust Multiplex Analysis and Pattern-Based Identification of Allelic Variants", Human Mutation, 1999; 13:318-327				
2	Lee, et al. "Human KVLQT1 gene shows tissue-specific imprinting and encompasses Beckwith-Wiedemann Syndrome chromosomal rearrangements", <i>Nature Genetics</i> , Feb. 1997; 15:181-185				
V	Liu, et al. "New Mutations in the KVLQT1 Potassium Channel That Cause Long-QT Syndrome", Circulation, 1998; 97:1264-1269				
9_	Mannens, et al. "KVLQT1, the rhythm of imprinting", Nature Genetics, Feb. 1997; 15:113-115				
2	Marx, J. "Rare Heart Disease Linked to Oncogene", Research News, May 3, 1991; p. 647				
2	Neyroud, et al. "A novel mutation in the potassium channel gene KVLQT1 causes the Jervell and Lange-Nielsen cardioauditory syndrome", <i>Nature Genetics</i> , Feb. 1997; 15:186-189				
2	Priori, S.G. "Is long QT syndrome entering the era of molecular diagnosis?", Heart, 1997; 77:5-6				
1	Priori, et al. "A Recessive Variant of the Romano-Ward Long-QT Syndrome?", Circulation, 1998; 97:2420-2425				
1	Rakaf, et al. Case Report - "Jervell and Lange-Nielsen QT syndrome: a case report from Saudi Arabia", International Journal of Pediatric Otorhinolaryngology, 1997; 39:163-168				
2	Romey, G. et al. "Molecular Mechanism and Functional Significance of the MinK Control of the KVLQT1 Channel Activity", The Journal of Biological Chemistry, July 4, 1997; 272(27):16713-16716				
~	Rosen. "Long QT Syndrome Patients with Gene Mutations", Circulation, 1995; 92:3373-3375				
0	Russell, M.W. et al. "KVLQT1 mutations in three families with familial or sporadic long QT syndrome", Human Molecular Genetics; 1996; 5(9):1319-1324				
a -	Saarinen, et al. "Molecular Genetics of the Long QT Syndrome: Two Novel Mutations of the KVLQT1 Gene and Phenotypic Expression of the Mutant Gene in a Large Kindred", <i>Human Mutation</i> , 1998; 11:158 165				
2	Sanguinetti, M.C. et al. "Coassembly of K _s LQT1 and minK (IsK) proteins to form cardiac I _{ks} potassium channel", <i>Nature</i> , Nov. 7, 1996; 384:80-83				
2	Sanguinetti, et al. "Review - Potassium Channelopathies", Neuropharmacology, 1997; 36(6):755-762				
2	Shimizu, et al. "Improvement of Repolarization Abnormalities by a K* Chanel Opener in the LQT1 Form of Congenital Long-QT Syndrome", Circulation, 1998; 97:1581-1588				
2	Splawski, et al. "Molecular Basis of the Long-QT Syndrome Associated with Deafness", <i>The New England Journal of Medicine</i> , May 29, 1997; 336(22):1562-1567				
2	Tanaka, et al. "Four Novel KVLQT1 and Four Novel HERG Mutations in Familial Long-QT Syndrome", Circulation, Feb. 4, 1997; 95(3):565-567				
2	Towbin, J.A. et al. "Evidence of Genetic Heterogeneity in Romano-Ward Long QT Syndrome", Circulation 1994; 90:2635-2644				
2	Tyson, J. et al. "IsK and KVLQT1: mutation in either of the two subunits of the slow component of the delayed rectifier potassium channel can cause Jervell and Lange-Nielsen syndrome", <i>Human Molecular Genetics</i> , 1997; 6(12):2179-2185				
EXAMINER 7	on con	DATE CON	ISIDERED //- 20	_0)	

EXAMINER: Initial if reference considered, whether or not citation is in conformation with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form 1449			heet <u>3</u> of		
PEZ	U.S. Department of Comm Patent and Trademark (nerce ATTY. DOCKET NO. 2323-151	SERIAL NO. 09/597,732		
O S MODE	TOF MATERIALS CITED BY APPLICANT (Use several sheets if necessary)	APPLICANT Mark T. KEATING et al.			
\$E 8	<u>/</u>	FILING DATE 19 June 2000	GROUP 1646		
4 FAT & THEORY	NON-PATENT DOCUMENTS (Including Author,	Title, Date, Pertinent Pages, Etc.	.)		
2	van den Berg et al. "The long QT Syndrome: a not gene", Hum. Genet., 1997; 100:356-361	vel missense mutation in the S6 r	egion of the KVLC		
V	/incent "Genetics and Molecular Biology of the Inherited Long QT Syndrome", Annals of Medicine, 1 6:419-425				
gr-	Vincent "The Molecular Genetics of the Long QT Annu. Rev. Med., 1998; 49:263-274	Syndrome: Genes causing faint	ting and sudden de		
2	Wang, Q. et al. "Molecular genetics of long QT syn Cardiology, 1997; 12:310-320	drome from genes to patients", C	Current Opinion in		
2	Wang, Q. et al. "Positional cloning of a novel potas arrhythmias", Nature Genetics, Jan. 1996; 12:17-2:	ssium channel gene: KVLQT1 m	nutations cause ca		
2	Wollnik, et al. "Pathophysiological mechanisms of c found in inherited cardiac arrhythmias", <i>Human Mo</i>	Iominant and recessive KVLQT1	K* channel mutati		
	Yang, et al. "KVLQT1, a voltage-gated potassium c Proc. Natl. Acad. Sci. USA, April 1997; 94:4017-40:		rdiac arrhythmias"		
2	GenBank Accession No. U86146 (1997)				
AMINER					
704		NSIDERED //- 20 - 0)			
AMINER: Initial if on the conformance	reference considered, whether or not citation is in cont and not considered. Include copy of this form with ne	formation with MPEP 609; Draw I	ine through citation		